

31

pentanoic acid ethyl ester is prepared at room temperature by dissolving 114 mg of the calcium salt of valsartan and 86 mg of (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester free acid in 2 mL methanol, followed by methanol evaporation. The glassy solid residue is then charged with 3 mL of acetonitrile and equilibrated by 10 min. sonication, followed by 20 hours of magnetic stirring.

Approximately 120 mg of white solids are collected by filtration. Liquid chromatography (LC) and elemental analysis indicate 1:1 ratio between (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester and valsartan. The sample is amorphous by X-ray powder diffraction.

Preparation of Linked Pro-Drug of Scheme (2)

Linked pro-drug of valsartan calcium salt and (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester and Tris is prepared at room temperature by dissolving 57 mg of the calcium salt of valsartan, 43 mg of (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester free acid, and 12.6 mg of tris(hydroxymethyl)aminomethane (Tris) in 2 mL methanol, followed by methanol evaporation. The glassy solid residue is then charged with 3 mL of acetonitrile and equilibrated by 10 min. sonication, followed by 20 hours of magnetic stirring. Approximately 83 mg of white solids are collected by filtration. LC and elemental analysis indicate 1:1 ratio between (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester and valsartan. The sample is amorphous by X-ray powder diffraction.

While the invention has been described above with reference to specific embodiments thereof, it is apparent that many changes, modifications, and variations can be made without departing from the inventive concept disclosed herein. Accordingly, it is intended to embrace all such changes, modifications and variations that fall within the spirit and broad scope of the appended claims. All patent applications, patents, and other publications cited herein are incorporated by reference in their entirety.

What is claimed is:

1. Trisodium [3-((1S,3R)-1-biphenyl-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl)propionate-(S)-3'-methyl-2'-(pentanoyl{2''-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}amino)butyrate] hemipentahydrate in crystalline form.

2. The compound of claim 1 having the sum formula $C_{48}H_{55}N_6O_8Na_3 \bullet 2.5 H_2O$ and being in the form of an asymmetric unit comprising six $C_{48}H_{55}N_6O_8Na_3 \bullet 2.5 H_2O$ formula units.

3. The compound of claim 1 characterized by an Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) spectrum having the following absorption bands expressed in reciprocal wave numbers (cm^{-1})($\pm 2 cm^{-1}$): 1711 (st), 1637 (st), 1597 (st) and 1401 (st).

4. The compound of claim 3 characterized by an Attenuated Total Reflection Fourier Transform Infrared (ATR-

32

FTIR) spectrum having the following absorption bands expressed in reciprocal wave numbers (cm^{-1})($\pm 2 cm^{-1}$):

2956 (w), 1711 (st), 1637 (st), 1597 (st), 1488 (w), 1459 (m), 1401 (st), 1357 (w), 1295 (m), 1266 (m), 1176 (w), 1085 (m), 1010 (w), 942 (w), 907 (w), 862 (w), 763 (st), 742 (m), 698 (m), 533 (st).

5. The compound of claim 1 characterized by an X-ray powder diffraction pattern taken with a Scintag XDS2000 powder diffractometer comprising the following interlattice plane intervals:

d in [Å] (± 0.1 Å): 21.2(s), 17.0(w), 7.1(s), 5.2(w), 4.7(w), 4.6(w), 4.2(w), 3.5(w), 3.3(w).

6. The compound of claim 1 characterized by an X-ray powder diffraction pattern taken with a Scintag XDS2000 powder diffractometer comprising the following interlattice plane intervals:

2θ in [°] 4.5, 5.5, 5.6, 9.9, 12.8, 15.7, 17.0, 17.1, 17.2, 18.3, 18.5, 19.8, 21.5, 21.7, 23.2, 23.3, 24.9, 25.3, 27.4, 27.9, 28.0, 30.2.

7. The compound of claim 1 in the form of a monoclinic unit cell, wherein its cell content comprises twelve formula units of $C_{48}H_{55}N_6O_8Na_3 \bullet 2.5 H_2O$.

8. The compound of claim 7 in the form of a monoclinic unit cell, wherein the cell content of the monoclinic unit cell comprises two asymmetric units on two-fold positions.

9. The compound of claim 7 wherein the monoclinic unit cell has a P2₁ space group.

10. The compound of claim 1 characterized by

sum formula	$C_{48}H_{55}N_6O_8Na_3 \bullet 2.5 H_2O$
molecular mass	957.99
crystal colour	colourless
crystal shape	tabular; hexagonal
crystal system	monoclinic
space group	P2 ₁
Cell parameters	a = 20.344 Å b = 42.018 Å c = 20.374 Å $\alpha = 90^\circ$ $\beta = 119.29^\circ$ $\gamma = 90^\circ$ 15190.03 Å ³
volume of unit cell	
Z (the number of asymmetric units in the unit cell)	2
calculated density	1.26845 g/cm ³ .

11. A pharmaceutical composition comprising an effective amount of the compound of claim 1 and at least one pharmaceutically acceptable additive.

12. The pharmaceutical composition of claim 10 further comprising a therapeutic agent selected from an anti-diabetic, a hypolipidemic agent, an anti-obesity agent and an anti-hypertensive agent.

13. The pharmaceutical composition of claim 11 wherein the therapeutic agent is amlodipine besylate.

14. The pharmaceutical composition of claim 11, wherein the therapeutic agent is hydrochlorothiazide.

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